

We claim:

1. A substantially pure or isolated oligodeoxynucleotide of at least about 16 nucleotides in length comprising a sequence represented by the following formula:

5' $X_1X_2X_3$ Pu₁ Py₂ CpG Pu₃ Py₄ $X_4X_5X_6(W)_M(G)_N$ -3'

wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10.

10 2. The oligodeoxynucleotide of claim 1, wherein N is about 6.

3. The oligodeoxynucleotide of claim 1 wherein Pu Py CpG Pu Py comprises phosphodiester bases.

15 4. The oligodeoxynucleotide of claim 3 wherein Pu₁ Py₂ CpG Pu₃ Py₄ are phosphodiester bases.

5. The oligodeoxynucleotide of claim 3, wherein $X_1X_2X_3$ and $X_4X_5X_6(W)_M(G)_N$ comprise phosphodiester bases.

20 6. The oligodeoxynucleotide of claim 3, wherein $X_1X_2X_3$ comprises one or more phosphothioate bases.

25 7. The oligodeoxynucleotide of claim 3, wherein $X_4X_5X_6(W)_M(G)_N$ comprises one or more phosphothioate bases.

8. The oligodeoxynucleotide of claim 1, wherein $X_1X_2X_3$ Pu Py and Pu Py $X_4X_5X_6$ are self complementary.

30 9. The oligodeoxynucleotide of claim 1, wherein $X_1X_2X_3$ AND $X_4X_5X_6$ are self complementary.

10. The oligodeoxynucleotide of claim 1, wherein Pu Py and Pu Py are self complementary.

11. The oligodeoxynucleotide of claim 1, wherein the
5 oligodeoxynucleotide comprises the sequence

5'-X₁X₂TGCATCGATGCAGGGGGG-3' (SEQ ID NO:12);
5'- X₁X₂TGCACCGGTGCAGGGGGG-3' (SEQ ID NO:13);
5'- X₁X₂TGCGTCGACGCAGGGGGG-3'; (SEQ ID NO:15);
5'- X₁X₂TGCGTCGATGCAGGGGGG -3'; (SEQ ID NO:16);
10 5'- X₁X₂TGCGCCGGCGCAGGGGGG-3'; (SEQ ID NO:17);
5'- X₁X₂TGCGCCGATGCAGGGGGG-3' (SEQ ID NO:18);
5'- X₁X₂TGCATCGACGCAGGGGGG-3' (SEQ ID NO:19); or.
5'- X₁X₂TGCGTCGGTGCAGGGGGG-3' (SEQ ID NO:20),
wherein X₁ is a G or not base and X₂ is a G or no base.

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12. The oligodeoxynucleotide of claim 1, comprising any one of
GGTGCATCGATGCAGGGGGG (SEQ ID NO: 1);
AAGGTCAACG TTGAAAAAAA (SEQ ID NO: 35);
20 GGTGCATCGATGCAGGGGGG (SEQ ID NO: 1);
GGTGCATCGATGCAGGGGGG (SEQ ID NO: 1);
GGTGCGTCGACGCAGGGGGG SEQ ID NO: 31);
GGTGCGTCGATGCAGGGGGG (SEQ ID NO: 7);
GGTGCAACCGGTGCAGGGGGG (SEQ ID NO: 2);
25 GTCGACGTCGAC (SEQ ID NO: 54);
GGTGCATCGATGCAGGGGGG (SEQ ID NO: 73);
GGCGTCGACG GGG (SEQ ID NO: 74);
GGTGCATCGATGCGAGAGA (SEQ ID NO: 87);
TCGGATGTTCTC (SEQ ID NO: 113), or
30 GGTCCATCGATCCAGGGGGG (SEQ ID NO: 138).

13. The oligodeoxynucleotide of any of claim 1, wherein the oligodeoxynucleotide is modified to prevent degradation.

14. The oligodeoxynucleotide of claim 1, wherein the oligodeoxynucleotide has a phosphate backbone modification.

15. The oligodeoxynucleotide of claim 14, wherein the phosphate backbone modification is a phosphorothioate backbone modification.

5 16. The oligodeoxynucleotide of claim 1, wherein the oligodeoxynucleotide comprises about 100 nucleotides or less.

17. The oligodeoxynucleotide claim 16, wherein the oligodeoxynucleotide comprises about 50 nucleotides or less.

10 18. The oligodeoxynucleotide of claim 9, wherein the oligodeoxynucleotide comprises about 18 to about 30 nucleotides.

19. An oligodeoxynucleotide delivery complex comprising the oligodeoxynucleotide of claim 1 and a targeting moiety.

15 20. The oligodeoxynucleotide delivery complex of claim 19, wherein the targeting moiety is selected from the group consisting of a cholesterol, a virosome, a liposome, a lipid, and a target cell specific binding agent.

21. The oligodeoxynucleotide of delivery complex of claim 19, wherein the oligodeoxynucleotide and the targeting moiety are covalently linked.

22. A pharmacological composition comprising the oligodeoxynucleotide of claim 1 and a pharmacologically acceptable carrier.

20 23. A method of stimulating a cell of the immune system, comprising contacting the cell with an effective amount of the oligodeoxynucleotide of claim 1, thereby stimulating the cell.

24. The method of claim 23, wherein the cell is a monocyte, a natural killer cell, or a dendritic cell.

25. A method of inducing an immune response in a subject, comprising administering a therapeutically effective amount of the oligodeoxynucleotide of claim 1, thereby inducing an immune response.

26. The method of claim 25, wherein the immune response
5 comprises a cell-mediated immune response.

27. The method of claim 25, wherein the immune response comprises a natural killer cell, or a dendritic cell response.

28. The method of any of claims 25, wherein the oligodeoxynucleotide induces production of a cytokine in the subject.

10 29. The method of claim 25, wherein the cytokine is interferon gamma (IFN- γ).

30. The method of claim 25, wherein the cytokine is interferon alpha (IFN- α).

15 31. The method of claim 25, wherein the cytokine is interferon inducible protein 10 (IP-10).

32. The method of claim 25, wherein the cytokine is interleukin 10 (IL-10).

20 33. The method of claim 25, wherein the immune response comprises activating or inducing maturation of a cell of the immune system, and wherein the cell of the immune system is an NK cell, a monocyte, a dendritic cell precursor or a dendritic cell.

34. The method of claim 33, wherein the immune response comprises activating a cell of the immune system, and wherein the cell of the immune system is an NK cell.

35. The method of claim 33, wherein the immune response comprises activating a cell of the immune system, and wherein the cell of the immune system is a monocyte.

5 36. The method of claim 33, wherein the immune response comprises inducing maturation of a cell of the immune system, and wherein the cell of the immune system is a dendritic cell.

37. The method of claim 36, wherein the dendritic cell is a plasmacytoid dendritic cell.

10 38. The method of claim 25, wherein the immune response is an immunotherapeutic response against a neoplasm.

39. The method of claim 38, wherein the neoplasm is a solid tumor.

40. The method of claim 38, further comprising administering an anti-neoplastic agent to the subject.

15 41. The method of claim 36, wherein the anti-neoplastic agent is a chemotherapeutic agent or radiation.

42. A method of inducing of an immune response to prevent or ameliorate an allergic reaction, comprising administering a therapeutically effective amount of the oligodeoxynucleotide of claim 1 to a subject having or subject to having an allergic reaction, wherein administration of the
20 oligodeoxynucleotide treat, prevents or ameliorates the allergic reaction.

43. The method of claim 42, further comprising administering an anti-allergenic agent.

44. The method of claim 42, wherein the allergic reaction is an asthmatic response to an allergen.

45. A method of enhancing the efficacy of a vaccine in a subject, comprising administering the oligodeoxynucleotide of claim 1 in combination with the vaccine to the subject, thereby enhancing the efficacy of the vaccine.

46. The method of claim 45, wherein the vaccine is a live, attenuated,
5 or heat-killed vaccine.

47. The method of claim 45, wherein the vaccine is a viral vaccine.

48. A method of preventing or treating a disease associated with an immune system in a subject, comprising administering a therapeutically effective amount of the oligodeoxynucleotide of claim 1 to the subject, wherein
10 administration of the oligodeoxynucleotide treats or prevents the disease associated with the immune system.

49. The method of claim 48, wherein the disease associated with the immune system is an autoimmune disorder.

50. The method of claim 48, wherein the disease associated with
15 the immune system is an immune system deficiency.

51. The method of claim 48, further comprising administering an anti-infectious agent.

52. A method of inducing an immune response against an infectious agent, comprising administering the oligonucleotide of claim 1 to a subject
20 infected with the infectious agent, thereby inducing an immune response against the infectious agent.

53. The method of claim 52, wherein the infectious agent is leishamanaisis.

54. The method of claim 52, wherein the infectious agent is a fungus,
25 bacteria, or a virus.

55. The method of claim 52, further comprising administering an anti-infectious agent.

56. The method of claim 52, wherein the anti-infectious agent is an antibiotic, an antiviral, or an anti-fungal agent.

5 57. A method for inducing an immune response in a subject, comprising

(a) contacting a monocyte or a dendritic cell precursor *in vitro* with the oligodeoxynucleotide of claim 1 to produce an activated antigen presenting cell, and

10 (b) administering the activated antigen presenting cell obtained in step (a) to the subject, thereby inducing an immune response.

15 58. A method for inducing an immune response in a subject, comprising

(a) contacting a monocyte or a dendritic cell precursor *in vitro* with the oligodeoxynucleotide of claim 1 to produce an activated antigen presenting cell, and

20 (b) contacting lymphocytes or natural killer cells *in vitro* with the activated antigen presenting cells to produce activated lymphocytes or activated natural killer cells; and

(c) administering the activated lymphocytes natural killer cells to the subject, thereby inducing the immune response.

25 59. The method of claim 58, wherein the monocytes or a dendritic cell precursors contacted *in vitro* with the oligodeoxynucleotide